WEST

Generate Collection

L11: Entry 2 of 30 File: USPT Mar 13, 2001

US-PAT-NO: 6200758
DOCUMENT-IDENTIFIER: US 6200758 B1

TITLE: Phenylalanine hydroxylase gene variants, and amino acid and pterin homeostasis, in the definition, detection, treatment and prevention of psychotic, mood and personality disorders

DATE-ISSUED: March 13, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Richardson; Mary Ann	New York	NY	N/A	N/A

US-CL-CURRENT: 435/6; 435/810

CLAIMS:

What is claimed:
1. A method of detecting a pathophysiological subtype of Psychotic Disorders, or if a person is at increased risk of developing a Psychotic Disorder comprising obtaining a biological sample from the person and detecting the presence or absence of a sequence alteration in phenylalanine hydroxylase (PAH) genomic DNA, wherein the presence of a mutation (Seq I.D.'s 37-38) or a polymorphism (Seq I.D.'s 27-36) is indicative of a pathophysiological subtype of Psychotic Disorder or of an increased risk of said disorders.
2. The method of claim 1, wherein a pathophysiological subtype of Schizophrenia is detected in persons with the disorder by the method comprising obtaining a biological sample from the person and detecting the presence or absence of a sequence alteration in phenylalanine hydroxylase (PAH) genomic DNA, wherein the presence of a K274E mutation (Seq I.D. 37) or an L321L polymorphism (Seq I.D. 33) is indicative of a pathophysiological subtype of Schizophrenia, wherein said person is of African ethnicity.
3. The method of claim 1, wherein a person at increased risk of developing Schizophrenia is detected by the method comprising obtaining a biological sample from the person and detecting the presence or absence of a sequence alteration in phenylalanine hydroxylase (PAH) genomic DNA, wherein the presence of a K274E mutation (Seq I.D. 37) or an L321L polymorphism (Seq I.D. 33) is indicative of a greater risk for developing Schizophrenia, wherein said person is of African ethnicity.
4. The method of claim 1, wherein the disorder is associated with hyperphenylalanemia.
5. The method of claim 1, 2, or 3, wherein the method further comprises amplifying the sequence-altered PAH DNA by use of the

polymerase chain reaction (PCR).
6. The method of claim 5, wherein the method further comprises analyzing the amplified DNA by denaturing gradient gel electrophoresis.
7. The method of claim 5, wherein the method further comprises analyzing the amplified DNA by single stranded conformation polymorphism.
8. A method of detecting a pathophysiological subtype of Psychotic Disorder, or if a person is at increased risk of developing a Psychotic Disorder, the method comprising
a) obtaining genomic DNA from a person, contacting the DNA samples independently with a pair of oligonucleotide primers (SEQ I.D.'s 1-26 or 39-62) capable of hybridizing to the human PAH gene sequence, incubating a hybridized pair of oligonucleotide primers in the DNA samples to produce DNA copies, and detecting in the sample DNA copies, a deviant electrophoretic pattern as being indicative of a sequence alteration in the PAH genomic DNA; wherein the psychotic disorder is Schizophrenia.
9. The method of claim 8 for detecting if a first or second degree relative is at increased risk of developing a Psychotic Disorder, comprising determining in a person diagnosed as having a Psychotic Disorder, the presence of a PAH variant (Seq I.D.'s 27-38), wherein from said first or second degree relative of said affected person, DNA samples are analyzed for said PAH variants.
10. The method of claim 8 for detecting if a first or second degree relative is at increased risk of developing Schizophrenia, comprising determining in a person of African ethnicity diagnosed as having Schizophrenia, the presence of the K274E mutation or L321L polymorphism, wherein from said first or second degree relative of said Schizophrenic person, DNA samples are analyzed for said PAH variants.
11. An isolated nucleic acid comprising the DNA sequence selected from the group consisting of SEQ ID Nos. 29, 30, 33, 36 or 37.

WEST

End of Result Set

Generate Collection

L11: Entry 30 of 30 File: USPT Oct 26, 1993

DOCUMENT-IDENTIFIER: US 5256533 A
TITLE: As a probe of serotonin uptake harmaline

BSPR:
The activity of serotonin, norepinephrine, acetylcholine, dopamine, opiate, tryptamine, and benzodiazepine systems play a significant role in many psychiatric disorders. For example, serotonin receptor number and uptake site activity changes in the pathological states of schizophrenia, depression, suicidal behavior, and others (Stahl et al. 1985). For patients with major affective depression, drugs which alter the uptake site activity of norepinephrine and serotonin, "tricyclic antidepressants" offer the mainstay of effective treatment. No generally effective method for the accurate assessment of these sites needed for the diagnosis and more importantly the effective management of these patients currently exists.

BSPR:
Because of the inaccessibility of brain tissue, many of the receptor and uptake sites of interest are impractical to analyze. However, lymphocytes and platelets are alternative tissue sources that contain serotonin uptake and receptor sites (Stahl et al. 1985). Human platelets are perhaps the best developed peripheral model and the most extensively studied. They are rich in serotonin receptors and uptake sites (Stahl and Meltzer 1978; Sneddon et al. 1969, 1971, 1973; paul et al. 1980, 1981a) as well as imipramine binding sites (Briley et al. 1979) (some authors have hypothesized a closely associated but separate receptor for serotonin and imipramine, a potent pharmacologic serotonin uptake inhibitor, while other authors present a single site model). Platelets, like lymphocytes, have monoamine oxidase, alpha-2 adrenergic receptors, and Na/K ATPase. In addition lymphocytes are rich in beta-adrenergic receptors. The receptor/uptake systems of platelets and of central nervous system have been suggested by others to be analogous in view of the many demonstrated similarities.

BSPR:
For instance, in major depressive disorders the capacity and number of serotonin uptake sites is decreased in platelets as well as in central nervous system tissue (Justice et al. 1988; Briley et al. 1980: Paul et al. 1981b; Stanley et al. 1982). Fluorescent cell sorting (Flow cytometry) is a recognized tool which, through recent developments, can measure kinetics of bound and unbound ligands in equilibrium using fluorescent labeling